

**AMENDMENT UNDER 37 C.F.R. § 1.114(c)**  
**U.S. Application No. 10/527,708 (Q101073)**

**AMENDMENTS TO THE CLAIMS**

**This listing of claims will replace all prior versions and listings of claims in the application:**

**LISTING OF CLAIMS:**

1-14. (Cancelled).

15. (Currently Amended) A method of screening for a drug candidate compound or its salt ~~wherein said drug candidate compound or its salt inhibits the activity of~~ by inhibiting neuronal cell expression of a gene encoding a protein comprising the amino acid sequence of SEQ ID NO:1 wherein neuronal cell death is induced by endoplasmic reticulum stress,

wherein said compound or its salt is ~~a candidate for a prophylactic or therapeutic agent for neurodegenerative disease or diabetes~~ an antisense polynucleotide, a double-stranded RNA or a ribozyme,

wherein said method comprises:

(i) culturing a neuronal cell comprising a polynucleotide encoding said protein in the presence of a cell death inducer for the endoplasmic reticulum stress;

(ii) culturing a neuronal cell comprising the polynucleotide in the presence of a ~~test~~ the compound and said cell death inducer;

(iii) assaying the degree of changes in nerve fibers to determine the neurofibrillary degeneration promoting activity in steps (i) and (ii); wherein said assaying comprises comparing said changes.

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16-53. (Cancelled).

54. (New) The method according to claim 15, wherein the neural cell is selected from a rat primary nerve cell, a rat hippocampal neuron and a human neuroblastoma SK-N-AS cell.

55. (New) The method according to claim 15, wherein the cell death inducer is selected from the group consisting of tunicamycin, thapsigargin, 2-deoxyglucose,  $\beta$ -amyloid, okadaic acid and homocysteine.

56. (New) The method according to claim 15, wherein the step (iii) comprises assaying:

the degree of changes in nerve fibers by immunostaining the nerve fibers using anti-tau antibody and microscopically examining the stained patterns,  
the degree of axonal degeneration by calcein staining,  
the mitochondrial respiratory activity,  
the LDH (lactate dehydrogenase) level in the culture supernatant, or  
the DNA break level accompanied by cell death.